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10/587,075	09/29/2006	Shu Kobayashi	2006_1192A	6955

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EXAMINER	
KOSACK, JOSEPH R	

ART UNIT	PAPER NUMBER
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,075	KOBAYASHI, SHU	
	Examiner	Art Unit	
	Joseph R. Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-7 are pending in the instant application.

Priority

The claim to priority as a 371 filing of PCT/JP05/01282, filed on January 24, 2005, which claims benefit of JP 2004-016407 filed on January 23, 2004, is acknowledged, but only granted in part. The claim to PCT/JP05/01282 is granted. However, the further claim of foreign priority to JP 2004-016407 is only acknowledged since the priority document is not in English and an intervening reference can be applied against the claims.

Information Disclosure Statement

There are no Information Disclosure Statements filed in the instant application.

Claim Rejections - 35 USC § 112

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method using catalysts with copper and chiral diamines where the chiral diamine is selected from the group on page 6 of the specification and the copper source is copper (II) source, does not reasonably provide enablement for a method using catalysts with any other chiral diamine or a copper (I) source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

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The Nature of the Invention

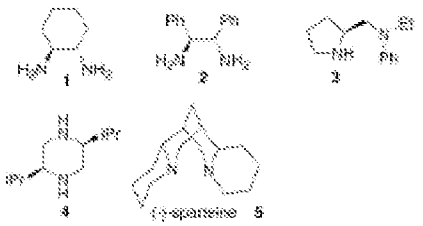
The nature of the invention is a method of performing an enantioselective nucleophilic addition reaction of an enamide to an imine by performing the reaction in the presence of a chiral copper catalyst. Dependent claims define structures for the enamide and imine compounds, as well as further define the catalyst to be formed by a copper compound which is a salt of an organic or inorganic acid and a chiral diamine ligand, which may or may not have an ethylene diamine structure as a portion thereof.

The State of the Prior Art and the Predictability or Lack Thereof in the Art

The state of the prior art is that the copper catalyzed enantioselective nucleophilic addition of enamide to an imine is not well known in the art. The only reference that the Examiner was able to find was Applicant's own work of Matsubara et al. (*Angewandte Chemie, Int. Ed. Eng, 2004,* 1679-1681.)

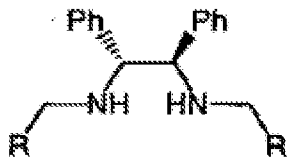
Matsubara et al. teach the instant process for the copper catalyzed enantioselective nucleophilic addition of enamide to an imine, but as the same with the

instant specification, only teach/exemplify using copper(II) triflate with a chiral 1,2-diphenyl-1,2-diamine compound to perform the reaction. See page 1679.

Li et al. (*Journal of Organic Chemistry, 2003,* 5500-5511) teach that the following chiral diamines:  , are the most widely used in asymmetric synthesis. See page 5501. This doesn't mean that they will work for every system, but only that these are the most widely used. Li et al. teach that various copper salts can be used in their process, but the catalyst used starts in the copper(II) oxidation state. For example, see page 5503, first paragraph, detailing how CuI was used to make the catalyst 7a·CuI(OH)·(H2O)x.

Therefore, the person of skill in the art would conclude that the choice of chiral diamine is critical in order to perform a coupling reaction enantioselectively. Additionally, the copper source must be chosen such that the oxidation state of the copper ion is proper to perform the reaction.

The Amount of Direction or Guidance Present and the Presence or Absence of Working Examples

The specification details examples of the process using the chiral diamine ligand:  , where R is 1-naphthyl, with copper (II) triflate as the copper

source, to enantioselectively couple enamides to imines. The process exemplifies different enamides and imines, however it is noted that all of the imines exemplified have a carbonyl group directly attached to the imine nitrogen. The Examiner does believe that the reaction would proceed if a carbonyl group was not directly attached to the nitrogen of the imine.

The Breadth of the Claims

The breadth of the claims is a method of performing an enantioselective nucleophilic addition reaction of any enamide to any imine by performing the reaction in the presence of any chiral copper catalyst. Dependent claims define structures for the enamide and imine compounds, as well as further define the catalyst to be formed by a copper compound which is a salt of an organic or inorganic acid and a chiral diamine ligand, which may or may not have an ethylene diamine structure as a portion thereof.

The Quantity of Experimentation Needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine all of the reaction conditions in order to possibly use other diamines, let alone any chiral ligand, and/or a copper source with a different oxidation state, such as a copper (I) source. The lack of predictability in the art to use disparate catalytic systsems as described above additionally supports a finding of undue experimentation.

The Level of Skill in the Art

The level of skill in the art of organic synthesis and pharmaceuticals is high. However, due to the unpredictability in the art as described above, one of ordinary skill

would be unable to make or use the claimed compound without undue experimentation in order to practice the invention as claimed.

Thus, the specification fails to provide sufficient support to enantioselectively couple an enamide to an imine with any chiral copper catalyst. As a result, the application would require one of skill to perform an exhaustive search and an inordinate number of experiments in order to make or use the claimed method.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which chiral copper catalysts can be used to perform the enantioselective coupling of enamides to imines.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

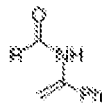
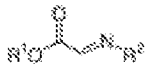
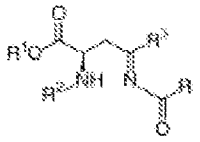
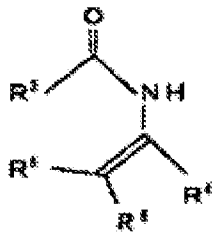
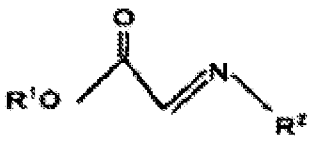
Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps for creating the reaction mixture and the step for performing the reaction.

Claim Rejections - 35 USC § 102

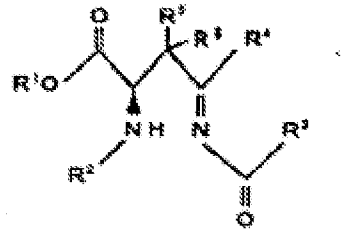
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticpated by Matsubara et al. (*Angewandte Chemie, Int. Ed. Eng, 2004,* 1679-1681.)

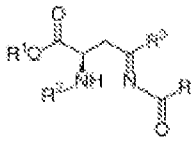
Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

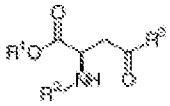
Matsubara et al. teach the reaction of an enamide,  , where R is OBn, with an imine,  , where R1 is ethyl and R2 is OC11H23, in the presence of a chiral copper catalyst which is formed by mixing copper (II) triflate with the chiral diamine,  , where R is 1-naphthyl, to form  , where the substituents are as described above. See page 1679, Scheme 1 and Table 1, entry 1. This reads on claims 1-4 where the chiral diamine ligand has an ethylene diamine structure as a portion thereof, the enamine is  , where R3 is a hydrocarbon group bonded via an oxygen atom, R4 is a hydrocarbon group, R5 and R6 are hydrogen, the imine is  , where R1 is a hydrocarbon group

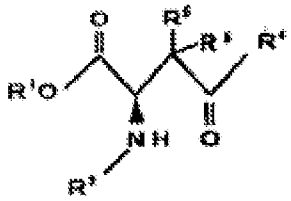
and R2 is R0-O, where R0 is a hydrocarbon group, and the final product is

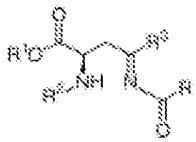
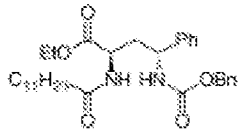


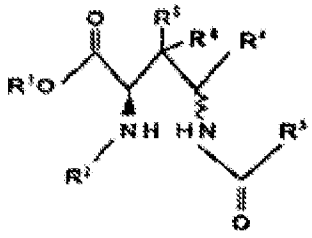
, where R1-R6 are as set forth above.

Matsubara et al. then teach the reaction of the  with acid to form

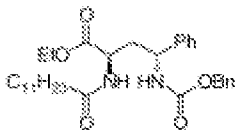
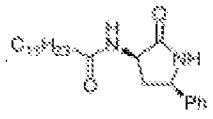
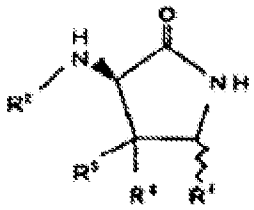


. See Scheme 1, step between compounds 4 and 5 on page 1679. This reads on claim 5 where the acid treatment forms the compound  , wherein R1 is a hydrocarbon group, R2 is R0-O, where R0 is a hydrocarbon group, R4 is a hydrocarbon group, and R5 and R6 are hydrogen.

Matsubara et al. then teach the reaction of  with a reducing agent to form  . See page 1680, Scheme 3. This reads on claim 6 where the



reduction forms the compound R1 is a hydrocarbon group, R2 is R0-O, where R0 is a hydrocarbon group, R3 is a hydrocarbon group bonded via an oxygen atom, R4 is a hydrocarbon group, and R5 and R6 are hydrogen.

Matsubara et al. finally teach the reaction of  wherein an acyl group is removed to form  . See page 1680, Scheme 3. This reads on claim 7 where an acyl group of a gamma-amino group of the optically active alpha,gamma-diamino acid ester is removed to form  R2 is R0-O, where R0 is a hydrocarbon group, R4 is a hydrocarbon group, and R5 and R6 are hydrogen.

Conclusion

Claims 1-7 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph R Kosack/
Examiner, Art Unit 1626